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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,869	11/29/2001	A. James Mixson	5627*6	9568

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,869	MIXSON, A. JAMES	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/24/81
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/11/04 has been entered.

Claims 21-40 are pending and under consideration in this Office Action.

Priority

This case is a continuation of 09/500,838, which is a continuation in part of 08/985,526, now abandoned, which is a continuation in part of 08/680,845, filed 12/5/97, now issued as US Patent 6,080,728. 08/985,526 provides no support for claims 21-35, which are directed to methods of inhibiting tumor growth through administration of RNA in a carrier that is either liposomes, cationic polymers, micelles. Additionally, the '728 patent provides no support for delivering RNA by liposomes, cationic polymers, micelles, or combinations of these carriers. For these reasons, the priority date for claims 21-35 is considered to be 2/10/00, the filing date of 09/500,838.

Instant claims 36-40 are drawn to methods of inhibiting tumor growth by administering in a carrier a "nucleic acid" encoding at least one anti-angiogenic protein. The scope of the term "nucleic acid" clearly embraces RNA as well as DNA. As

discussed above, of the priority documents, only 09/500,838 supports the scope of "nucleic acid" embracing RNA. As a result the priority date for claims 36-40 is also considered to be 2/10/00.

Rejections Withdrawn

After further consideration, the rejection of claims 21-35 under 35 U.S.C. 112, first paragraph is withdrawn in favor of new grounds of rejection under 35 USC 103.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 36-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,080,728 ('728). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Instant claim 36 is a method of inhibiting tumor growth in a subject bearing a tumor by administering a nucleic acid encoding at least one anti-angiogenic protein or peptide in a carrier selected from the group consisting of liposomes, cationic polymers, micelles, and a combination thereof. Instant claim 37 requires intravenous injection, and instant claims 38-40 require a liposomal carrier, a cationic polymer carrier, or a micelle carrier, respectively.

Claim 1 of '728 is drawn to a method of inhibiting tumor growth by administering to a subject a DNA encoding an anti-angiogenic protein with a carrier which may be a liposome, a micelle, or a cationic polymer. Claim 2 requires intravenous injection, and claims 3-5 require a liposomal carrier, a cationic polymer carrier, or a micelle carrier, respectively.

Accordingly claims 1-5 of '728 teach species (methods of delivering DNA) of the claimed genus (methods of delivering nucleic acids), rendering the instant claims obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 23-26, 28-36, and 38-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting tumor growth in a subject bearing tumor by administering intravenously, or directly into a

tumor, an RNA encoding at least one anti-angiogenic protein or peptide, wherein the RNA is administered in a carrier and is expressed and tumor growth is inhibited, wherein the carrier is selected from liposomes, cationic polymers, micelles, and a combination thereof, does not reasonably provide enablement for such methods in which administration is other than intravenous or intratumoral. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is a method of inhibiting tumor growth in a subject by administration of RNA encoding an anti-angiogenic protein or peptide. The specification indicates at paragraph 77 that administration may be by intravenous, subcutaneous or intratumoral injection. Thus the invention broadly read on methods of treating nonsubcutaneous, e.g. brain, liver, or pancreatic tumors, by subcutaneous administration of the RNA compositions.

One of ordinary skill in the art appreciates that subcutaneous administration of nucleic acid/carrier complexes is a local administration technique and will not result in delivery of nucleic acids to sites other than the administration site. In contrast, intravenous administration allows for systemic delivery. As such, one of skill in the art would not reasonably expect subcutaneous administration of the claimed complexes to result in inhibition of tumor growth in any tumor other than a subcutaneous tumor at the site of administration. For example, one could not reasonably expect to inhibit by subcutaneous administration growth of organ tumors such a brain, liver or pancreatic

tumors. As such it is suggested that the claims should be amended to require intratumoral or intravenous administration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Mixson (EP 0 819 758 A2, published 1/21/98).

Mixson teaches methods of inhibiting tumor growth in a subject bearing a tumor, which comprises intravenous or intratumoral injection of DNA encoding an anti-angiogenic peptide provided with a carrier selected from the group consisting of cationic lipids, liposomes, and cationic polymer carriers. Mixson also coadministers an expression vector for p53. See e.g. page 5, lines 24-26 and 33-38; page 15, lines 41-43; and page 17, lines 2-46.

Thus Mixson anticipates the claims.

The PTO recognizes that Applicant has a chain of support for DNA embodiments that includes Mixson (1998). This rejection is considered valid because the rejected claims have been assigned a priority date of 2/10/00, due to the fact that they are drawn to "nucleic acids" and therefore embrace matter not disclosed in the priority documents, e.g. RNA. This rejection could be overcome by limiting the scope of the claimed

nucleic acids to DNA, as disclosed in the priority documents. This would have the effect of changing the priority date assigned to the claims such that Mixson (1998) would not longer be available as prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-24, 26-31, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mixson (EP 0 819 758 A2, published 1/21/98) in view of Lu et al (Cancer Gene Therapy, 1(4): 245-252).

Mixson teaches methods of inhibiting tumor growth in a subject bearing a tumor, which comprises intravenous or intratumoral injection of DNA encoding an anti-angiogenic peptide provided with a carrier selected from the group consisting of cationic lipids, liposomes, and cationic polymer carriers. Mixson also coadministers an expression vector for p53. See e.g. page 5, lines 24-26 and 33-38; page 15, lines 41-43; and page 17, lines 2-46.

Mixson does not teach the use of RNA.

Lu teaches direct delivery to tumors in vivo of liposome/mRNA complexes, stating that liposome/DNA expression vector complexes and liposome/mRNA

complexes gave comparably transfection efficacy. See also Fig. 7 on page 251 which shows an approximate 2 fold difference in expression between DNA and RNA transfection in vivo.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute mRNA for DNA in the method of Mixson. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). In this case, mRNA is recognized in the art as having comparable efficacy to DNA for in vivo delivery and expression, so it would have been obvious to substitute one for the other.

Thus the invention as a whole was prima facie obvious.

Claims 25, 32, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mixson (EP 0 819 758 A2, published 1/21/98) and Lu et al (Cancer Gene Therapy, 1(4): 245-252), as applied to claims 21-24, 26-31, and 33-39, and further in view of Lee et al (US Patent 5,908,777, issued 6/1/99).

The teachings of Mixson and Lu are detailed above. These references do not explicitly teach a micelle carrier

Lee teaches that micelles are art-recognized equivalents of liposomes and cationic polymers. See Detailed Description paragraph 12 which states:

"The category of suitable cationic helper molecules is illustrated by (1) non-monovalent cations such as Ca.sup.2+, Mg.sup.2+, Mn.sup.2+, Al.sup.3+, and spermidine, (2) cationic polymers such as polylysine, DEAE-dextran, spermine, spermidine, protamine, polybrene, cationized proteins, cationic micelles and cationic liposomes, and (3) cationic detergents such as DC-chol, cetyltrimethylammonium bromide (CTAB), etc."

As stated above MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious.

Thus the invention as a whole was prima facie obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER